

**REMARKS**

Applicants have canceled claim 4 and have added new claims 10 and 11. Applicants have amended claims 1-3 and 5-9 to conform with U.S. claim requirements. Attached hereto is a marked-up version of the changes made by the current amendment, captioned "Appendix to the Preliminary Amendment." Specifically, Applicants have clarified the claims, changed claim dependency, and provided proper antecedent basis support. No new matter has been added by these amendments and support for the changes made is in the original claims and the specification. Claims 1-3, and 5-11 are pending.

If there is any fee due in connection with the filing of this Preliminary Amendment, please charge the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,  
GARRETT & DUNNER, L.L.P.

Dated: March 10, 2003

By: Carol P. Einaudi  
Carol P. Einaudi  
Reg. No. 32,220

FINNEGAN  
HENDERSON  
FARABOW  
GARRETT &  
DUNNER LLP

1300 I Street, NW  
Washington, DC 20005  
202.408.4000  
Fax 202.408.4400  
www.finnegan.com

**APPENDIX TO THE PRELIMINARY AMENDMENT**

1. A modified Factor VIII cDNA, wherein comprising:  
an at least one intron, which is not an FVIII intron, has been inserted into  
at least one location of the wild-type factor VIII cDNA, wherein said at least one intron is  
not a factor VIII intron; and

characterized in that as a promoter a cDNA is used which is suitable for  
targets the expression of said modified factor VIII cDNA to in hematopoietic cells lines  
and specifically in platelets.

2. Modified Factor VIII cDNA as claimed in Claim 1, ~~characterized in that~~  
wherein the B-domain of the wild-type factor VIII cDNA has been deleted.

3. Modified Factor VIII cDNA as claimed in Claim 21, ~~characterized in that~~  
wherein said at least one the intron, which is not an FVIII intron, is a truncated factor IX  
intron 1.

5. Modified Factor VIII cDNA as claimed in claim 41, ~~characterized in that~~  
wherein said as a promoter the cDNA coding for is the human platelet glycoprotein IIb  
(GPIIb) promoter is used.

6. Modified Factor VIII cDNA as claimed in claim 41, ~~characterized in that~~  
wherein said at least one intron the truncated factor IX intron 1 has been inserted into  
the wild-type factor VIII cDNA at the original positions of intron 1 and intron 13 of the  
genomic Factor VIII DNA introns 1 + 13.

FINNEGAN  
HENDERSON  
FARABOW  
GARRETT &  
DUNNER LLP

1300 I Street, NW  
Washington, DC 20005  
202.408.4000  
Fax 202.408.4400  
www.finnegan.com

7. A p~~P~~rocess for the production of Factor VIII, ~~characterized in that~~  
comprising:  
culturing a cell line under conditions suitable to produce a polypeptide  
encoded by the ~~production is performed in the cell line HEL or in the cell line Dami using~~  
a modified Factor VIII cDNA as claimed in claim 1; and  
recovering said polypeptide from the cell culture medium.
8. Process as claimed in claim 7, ~~characterized in that~~ wherein the  
production of Factor VIII is stimulated by an inducer.
9. Process as claimed in claim 8, ~~characterized in that~~ wherein said as  
inducer is phorbol-12-myristate-13-acetate (PMA) ~~is used.~~

FINNEGAN  
HENDERSON  
FARABOW  
GARRETT &  
DUNNER LLP

1300 I Street, NW  
Washington, DC 20005  
202.408.4000  
Fax 202.408.4400  
www.finnegan.com